REMARKS

Claims 41-52 and 59-78 are pending and are the subject of the instant Office Action.

In the amendment herein, Claims 41-52 and 59-68 have been cancelled without prejudice, acquiescence to any outstanding objections or rejections, or intention to surrender the full scope of subject matter embodied by the claims. Applicant respectfully reserves the right to prosecute claims directed to the subject matter of the now cancelled claims in future continuing applications.

Claims 79-87 have been added and are fully supported by the specification as filed.

Claim 69 has been amended, and these amendments are likewise fully supported by the specification as filed.

The amendments to the claims are illustrated on the attached page entitled "Marked Up Version to Show Changes Made". For the Examiner's convenience, a clean copy of all the now pending claims 69-87 is provided above.

Each of the objections and rejections set forth in the Office Action are addressed below.

Objection to Specification

The amendment filed December 13, 1999 was objected to under 35 USC Section 132 on grounds that it introduces new matter into the disclosure. Applicant respectfully disagrees.

It is believed that the Medical Dictionary definitions referred to in the Office Action do not establish that the pending claims introduce new matter into the instant application. Applicant's specification, originally filed on January 9, 1996, sufficiently provides a description and details so as to enable a person skilled in the art to make and use the invention. The specification as filed clearly sets forth the use of Apo-2 ligand as a cancer therapy in the context of a variety of different types of cancer. The effectiveness of Apo-2 ligand in inducing apoptosis in a wide array of different types of cancer cells (shown for instance in the working examples) establishes to the skilled artisan that the apoptotic activity of

Apo-2 ligand is not specific to just one type of cancer. Accordingly, the definition of "cancer" provided on page 12, lines 1-12 of the specification is not meant to be a "restrictive" list of the types of cancers contemplated by the invention. Those skilled in the art, reading the specification as drafted, will fully understand that the activity observed for Apo-2 ligand has application in a wide variety of cancers - not just those expressly listed in the definition.

Withdrawal of the rejection is hereby requested.

Section 103 Rejections

The Examiner has issued rejections of the pending claims under Section 103(a) predicated on the Examiner's position that the application is not entitled to its priority filing date and on the combined teachings of multiple references. Applicant respectfully traverses each of the Section 103(a) rejections.

Because these rejections involve the combinations of multiple references, Applicant is reproducing them below:

Claims 47-51 and 69-74 over Weller, Pitti, Chiocca, Chen;

Claims 47-52 and 69-76 over Weller, Pitti, Chiocca, Chen, Davis;

Claims 41-52, 59-66, and 69-76 over Weller, Pitti, Chiocca, Chen, Davis, Lutz, DiResta;

Claims 41-52 and 59-78 over Weller, Pitti, Chiocca, Chen, Davis, Lutz, DiResta, Wiley;

Claims 47, 51, 69, and 74 over Rieger and Pitti;

Claims 41-52 and 59-78 over Rieger, Pitti, Weller, Chiocca, Chen, Davis, Lutz, DiResta, Wiley.

Each of these rejections are defective on at least the following grounds. First, for the reasons above, it is Applicant's position

that the claims in the instant application are appropriately accorded entitlement to the application's January 9, 1996 priority filing date. Most of the references cited by the Examiner, including the Weller, Pitti, Wiley and Rieger references, are not even available as effective prior art against the instant application because they were published AFTER the filing date of the instant application.

Second, the shear number of references combined in these rejections demonstrates a piecemeal dissection of isolated teachings of each reference. There is nothing in these references which demonstrates a motivation to one skilled in the art to combine these teachings in the way suggested by the Examiner, and it is only with an impermissible use of hindsight that one could attempt to combine them in such a way to suggest the claimed invention.

Withdrawal of these rejections is respectfully requested.

Section 112 Rejections

Claims 41-52, 59-63, 65, 67-73, 75, 77 and 78 were rejected under Section 112, first paragraph as not being described sufficiently to show possession. This rejection is respectfully traversed.

The claims are directed to methods of using various forms of Apo-2 ligand, namely those polypeptides comprising amino acids 114-281 or fragments thereof. The claims provide that such polypeptides are used in an amount effective to induce cell death in the mammal's cancer cells. It is respectfully submitted that those skilled in the art fully understand the scope of polypeptides contemplated for use in the claimed invention. The structural and functional characteristics of the recited polypeptides are fully described in the specification and will be readily apparent to the skilled artisan.

Claims 59-63, 67-73, and 77-78 were rejected under Section 112, first paragraph, as being non-enabled for a polypeptide consisting of amino acids 1-281. Without acquiescence or intention to surrender the full scope of subject matter of these claims, the claims have been amended. It is believed this amendment renders this rejection moot.

Claims 41-52 were rejected under Section 112, second paragraph, as being indefinite. Without acquiescence or intention to surrender

the full scope of subject matter of these claims, claims 41-52 have been cancelled without prejudice. It is believed this amendment renders this rejection moot.

Respectfully submitted,
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In the claims:

Please cancel claims 41-52 and 59-68 without prejudice.

Please amend claim 69 as follows:

69. (Amended) A method of treating a mammal having [glioma or glioblastoma] a blastoma cancer, comprising administering to the mammal Apo-2 ligand polypeptide in an amount effective to induce cell death in the mammal's [glioma or glioblastoma] blastoma cells, wherein said Apo-2 ligand polypeptide is selected from the group consisting of:

(a) a polypeptide comprising amino acid residues 114-281 of Figure 1A (SEQ ID NO:1);

(b) a polypeptide consisting of amino acid residues 114-281 of Figure 1A (SEQ ID NO:1); and

(c) [a polypeptide consisting of amino acid residues 1-281 of Figure 1A (SEQ ID NO:1);

(d)] a polypeptide which is a fragment of (a)[,] or (b) [or (c)].

Please add the following claims:

--79. The method of claim 69 wherein said blastoma is glioblastoma multiforme.

80. A method of treating a mammal having glioblastoma multiforme, comprising administering to the mammal Apo-2 ligand polypeptide in an amount effective to induce cell death in the mammal's glioblastoma multiforme cells, wherein said Apo-2 ligand polypeptide is selected from the group consisting of:

(a) a polypeptide comprising amino acid residues 114-281 of Figure 1A (SEQ ID NO:1);

(b) a polypeptide consisting of amino acid residues 114-281 of Figure 1A (SEQ ID NO:1);

(c) a polypeptide which is a fragment of (a) or (b).

81. The method of claim 80 wherein said Apo-2 ligand polypeptide consists of amino acid residues 114-281 of Figure 1A (SEQ ID NO:1).

82. The method of claim 80 wherein said Apo-2 ligand polypeptide is linked to one or more nonproteinaceous polymers selected from the group consisting of polyethylene glycol, polypropylene glycol, and polyoxyalkylene.

83. The method of claim 80 wherein said Apo-2 ligand polypeptide is unglycosylated.

84. A method of treating a mammal having glioblastoma multiforme, comprising administering to the mammal Apo-2 ligand polypeptide in an amount effective to induce cell death in the mammal's glioblastoma multiforme cells, wherein said Apo-2 ligand polypeptide comprises amino acid residues 114-281 of Figure 1A (SEQ ID NO:1).

85. The method of claim 84 wherein said Apo-2 ligand consists of amino acid residues 114-281 of Figure 1A (SEQ ID NO:1).

86. The method of claim 84 wherein said Apo-2 ligand polypeptide is linked to one or more nonproteinaceous polymers selected from the group consisting of polyethylene glycol, polypropylene glycol, and polyoxyalkylene.

87. The method of claim 84 wherein said Apo-2 ligand polypeptide is unglycosylated. ---